PRIMARY CARCINOMA OF THE VERMIFORM APPENDIX, WITH A REPORT OF THREE CASES.[1]

BY ARTHUR W. ELTING, M.D.,

OF ALBANY, N. Y.,

Surgeon to the Child's Hospital; Lecturer on Surgical Pathology in the Albany Medical College.

THE exceedingly infrequent occurrence of primary malignant neoplasms of the vermiform appendix has long been a subject of comment among surgeons and pathologists. In the voluminous literature devoted to diseases of the appendix there are but comparatively few references to malignant diseases of this organ, and some of these are decidedly unauthentic. This appears to be especially true of the earlier cases reported. In order that some idea may be gained as to the accuracy of these observations, the writer has taken the trouble to look up the original reports, where such exist, of practically all the cases in the literature.

The first reference to carcinoma of the appendix is a case reported by Merling [1] in 1838. The report was of the findings at an autopsy upon a case which had died of general peritonitis. The wall of the appendix was thickened, scirrhous, and of a grayish-brown color. Furthermore, it appeared to be occupied by several small hard tumors. Near the attachment to the cæcum the appendix presented a small ragged opening the size of a pea, through which the intestinal contents had escaped into the peritoneal cavity. Although assumed to be a case of primary carcinoma of the appendix, no mention was made of a microscopical examination, and it would appear to be much more probable that it was a case of perforative appendicitis.

The next mention of primary carcinoma of the appendix

[1] Read before the New York State Medical Society, January 28, 1903.

was a case reported by Prus,[2] in 1865, of a woman of seventy-five years of age who died with symptoms of general peritonitis. At autopsy the peritonitis was found to have originated from a large perforation of the wall of the appendix. The mucous and muscular walls of the appendix were thickened. From the base of the ulceration about the perforation there sprang a small, soft sessile tumor, which on section showed some hæmorrhage. No mention was made of a microscopical examination, and it would also appear that this case was not one of primary carcinoma of the appendix.

The first important article upon the subject was that of Rokitansky,[3] who in 1867 reported four cases of what he believed to be primary carcinoma of the appendix. He called attention to the fact that prior to that time carcinomatous degeneration of the appendix had been scarcely recognized among the diseases of that organ.

The first case, which was observed in 1847, was that of an individual eighty-two years of age who died of pulmonary disease. At autopsy the appendix was found to be transformed into a sac six inches in length and two inches in diameter. It was situated to the outer and posterior side of the cæcum, to which it was densely adherent, and into the lumen of which it had caused a projection. The walls of the appendix appeared fibrous in character and the cæcal orifice of the appendix was obliterated. The sac which represented the degenerated appendix contained a yellowish white, opaque, gelatinous mass, which was streaked with blood. The wall of the sac consisted of fibrous tissue which had completely replaced the mucous and muscular coats, and upon the inner surface presented an areolated, reticulated appearance, the reticulæ traversing the gelatinous material and dividing it more or less into compartments.

The second case, observed in 1854, was that of an individual sixty-eight years of age who died of pneumonia. The appendix was two inches in length, and the distal two-thirds was transformed into a spindle-shaped fibrous sac about the size of a pigeon's egg, which contained a yellowish gelatinous material traversed by fine reticulated processes which took their origin from the wall of the sac.

The third case, observed in 1866, was that of an individual seventy years of age who died of heart disease. The appendix was four inches in length, and the distal, 2.9 inches, was transformed into a sac distended with a gray gelatinous material. This portion of the appendix was about one inch in diameter, and the wall, which was one-tenth of an inch in thickness, was of a fibrous character. The entire surface of this sac was smooth in some places, while in others it was irregular, and from it numerous delicate processes ran in different directions through the gelatinous material.

The fourth case, observed in 1866, was that of an individual thirty-eight years of age who died of pulmonary and intestinal tuberculosis. The appendix was 1.9 inches in length and consisted of two compartments. The distal, lined by a smooth mucosa, contained a grayish gelatinous material, while the proximal compartment was distended with a gelatinous material traversed by numerous delicate strands of tissue, which appeared to originate from the fibrous wall of the compartment. The walls of the appendix in this region appeared to be transformed into fibrous tissue.

Rokitansky concludes that this disease of the appendix consists of a stenosing colloid carcinomatous degeneration, which results in an enlargement and distortion of the organ and the transformation of its wall into a fibrous capsule. There is no discussion of the microscopical appearances of any of these specimens, and, hence, there is some question as to whether they were really instances of carcinoma, and not mucoid degeneration or dropsy of the appendix.

Kolaczek,[4] in 1875, reported a case of abscess in the right iliac fossa which opened and the fistula failed to heal. At autopsy a carcinoma of the cæcum was found, which connected with the fistula. The base of the appendix opened at the site of the ulcerated carcinoma, but no mention was made of involvement of the appendix.

This case is here mentioned because of the fact that it has been frequently referred to in the literature as an instance of primary carcinoma of the appendix, when it was very evidently an instance of primary carcinoma of the cæcum.

Leichtenstern,[5] in 1876, briefly mentioned statistically the observation of three carcinomata of the appendix. No mention, however, of the character of the neoplasms was made other than that they were carcinomata.

Bierhoff,[6] in 1880, reported a case of a woman of seventy-eight years who presented at autopsy carcinoma of the uterus and left ovary, as well as of the rectum, with metastatic nodules in the liver and spleen. The appendix was normal for three centimetres of the proximal portion. Three centimetres from the base was situated a carcinomatous nodule the size of a hazel-nut. This nodule produced an obstruction of the lumen such that the distal portion of the appendix was distended into a tense sac containing a grayish mucoid material. This case is here referred to because it, too, has been frequently quoted as an instance of primary carcinoma of the appendix, while in all probability the involvement of the appendix was secondary.

Beger,[7] in 1882, reported a case of considerable interest. The patient, a man of forty-seven years, developed three and one-half years previously a tumor in the right inguinal region, which was incised and about a litre of pus evacuated. The wound, however, never closed. No fæcal gases or intestinal contents appear to have escaped through the fistula. At operation the appendix was found attached by its tip to the base of the fistula, and occupied throughout its entire extent by a carcinomatous process. It was six centimetres in length and about the thickness of the finger. At the base of the appendix was a walnut-sized papillary tumor projecting into the cæcum, which presented the same structure as the rest of the new growth, and had evidently resulted from extension along the appendix. The patient died thirty-six hours after the operation, and at autopsy metastatic involvement of the retroperitoneal glands was found. Microscopical examination of the new growth showed it to be an adenocarcinoma. The writer believed the carcinoma to have begun at the tip and to have gradually extended to the base of the appendix. The case was of especial interest because of the absence of intestinal symptoms in spite of the existence of the tumor for so long a time.

Maydl,[8] in 1883, mentions one case of carcinoma of the appendix in an article upon intestinal carcinoma. No further men-

tion was made, however, of the gross or microscopical appearances of the tumor.

Draper,[9] in 1884, reported a case of a man of sixty-five years who died with obscure abdominal symptoms which did not allow of a clinical diagnosis. At autopsy the ileum above the ileocæcal valve was distended with liquid fæces. Just at the valve, upon its upper surface, three foreign bodies—two small fragments of bone and a prune-stone—were found lying loosely before the opening into the cæcum. The valve was constricted so as to admit the tip of the index-finger only with difficulty. The mucous membrane of the cæcum and lower part of the ascending colon was thickened and deeply reddened, but not ulcerated. The upper third or head of the appendix was enlarged and dilated to about the size of a large plum. The opening of the appendix into the intestine was also dilated. The thickened wall of this enlarged portion of the appendix presented the characteristic appearances of colloid disease. The free end of the appendix beyond the dilated portion was very slightly enlarged and contained inspissated fæcal matter. The peritoneum and subperitoneal tissues adjacent to the new growth were normal.

In this case there would appear to be a reasonable question as to whether the neoplasm may not have been primary about the ileocæcal valve and to have involved the appendix secondarily.

Lafforgue,[10] in 1893, presented an interesting thesis upon primary tumors of the appendix in which several cases in the literature were discussed and the clinical features of the disease were presented. The writer did not, however, report any additional cases.

Glazebrook,[11] in 1895, reported a case of so-called endothelial sarcoma of the appendix, which, because of the as yet unsettled relationship of these tumors to carcinoma, will be briefly referred to. The patient, a man of fifty-five years, died of cerebral hæmorrhage. At autopsy the appendix was in a normal situation, but bound down by dense adhesions. It was of normal size for three inches from the proximal end, at which point there was an enlargement the size and shape of a pigeon's egg, situated in the anterior wall of the appendix. The mass was hard and fibrous and resembled a scirrhous tumor. After microscopical examination, the tumor was said to be an endothelial sarcoma, the walls of the appendix being infiltrated by nests of irregular cuboidal or

cylindrical cells which were thought to be of endothelial origin. There were no evidences of metastases.

Stimson,[12] in 1896, reported a case of carcinoma of the appendix in a woman forty-four years of age, who had had a very severe attack of appendicitis ten years previously. She remained well until two months before operation, when she had a mild attack and recovered. Another mild attack led to an operation and the removal of the appendix, which was four inches in length and one inch in thickness, and presented a degenerated carcinoma, the type of which was not mentioned.

Letulle and Weinberg,[13] in 1897, presented a brief discussion of the subject of obliterating appendicitis, based upon the study of twelve cases, two of which presented primary carcinomata of the appendix. They called especial attention to the development of carcinoma in the fibrous cicatrix of an obliterated appendix and the involvement of all the layers of the appendix by the carcinoma. In one of their cases, both of which occurred in individuals dead of tuberculosis, they were able to demonstrate the starting-point of the carcinoma at the line of fusion where the lumen had been obliterated. In this case the carcinoma had extended from this point through the different layers to the peritoneum. In the second case the terminal extremity of the appendix was the seat of a peculiar adenomatous hypertrophy. The carcinoma had begun in the scar and had involved all the coats of the appendix.

Mossé and Daunic,[14] in 1897, reported a case of primary carcinoma of the appendix, found at autopsy upon a woman fifty years of age, dead of heart disease. There had been, so far as was known, no symptoms of appendicular disease. The appendix pointed downward and inward, was free from adhesions, and was provided with a normal-looking mesentery. It was four centimetres in length and much thicker than normal, having a maximum circumference of forty-five millimetres, cylindrical in shape, about the size of a date and largest at its free extremity. The consistency was firm and the surface smooth. The tumor was entirely confined to the appendix, and was situated for the most part in the mucosa, and in the centre of the growth was the lumen, which was much reduced in size. The mucosa was quite extensively invaded, the musculature less so, while the peritoneum appeared to be uninvolved. In the vicinity of the lumen vestiges

of the glands of Lieberkühn could be made out, some of which had undergone carcinomatous degeneration and seemed to have been the starting-point of the tumor. In portions of the section the tumor presented the appearance of a cylindrical-cell carcinoma, while in other portions it presented more of an alveolar arrangement. The absence of foci in the cæcum, lymphatic glands, and the other viscera led the writer to assume the tumor to be a primary carcinoma of the appendix.

Wright,[15] in 1898, reported an autopsy upon a case of general peritonitis of obscure origin. The autopsy failed to reveal any definite starting-point of the peritonitis. There were some adhesions about the appendix, but no definite evidence of perforation. Upon microscopical examination of the appendix a small primary carcinoma of the head of the organ was found, and just at the junction of the tumor with the wall of the gut was a small perforation which was doubtless the starting-point of the peritonitis. The tumor presented the microscopical appearances of a typical adenocarcinoma.

Monks,[16] in 1899, reported a case of tumor involving the cæcum, in the middle of which there was a slough which seemed to represent the appendix. The tumor proved to be a carcinoma and was undoubtedly primary in the cæcum, with possibly secondary involvement of the appendix. Reference is made to this case because it has been erroneously quoted as an instance of primary carcinoma of the appendix.

Nothnagel,[17] in 1898, briefly mentioned one case of carcinoma of the appendix observed in the Pathological Institute of the general hospital at Vienna. There was, however, no discussion of the characteristics of the case.

Zeman, of Vienna, has also mentioned statistically a case of carcinoma of the appendix, which, however, may be a case already referred to.

Hurdon,[18] in 1900, reported a case of a woman of twenty-four years, who, since the birth of her first child eight years previously, had had considerable pain in the lower abdomen and back, associated latterly with a constant aching in the right lumbar region. The uterus was found to be acutely retroflexed and operation advised. At operation the appendix was found to project downward over the brim of the pelvis and to be involved in dense adhesions. The appendix was removed, and the patient made a

good recovery. The appendix, which was ten centimetres in length, was found to be acutely flexed upon itself at about the junction of the middle and distal thirds. The proximal end was normal, but the distal end beyond the flexion was distended, and contained a soft concretion about the size of a date-stone. Joining the distended extremity to the normal proximal portion was an intermediary portion one and one-half centimetres in length, and of very firm consistence. This on section was found to be a small oval tumor ten by five millimetres, which had produced a marked stenosis of the lumen. Histologically, the tumor proved to be an adenocarcinoma which had invaded all the coats of the appendix. The patient was in excellent health at the time the report was made.

Letulle and Weinberg,[19] in a communication to the Anatomical Society of Paris in 1900, reported two additional cases of primary carcinoma of the appendix complicating chronic appendicitis. In the first case the carcinoma was discovered more or less accidentally in the course of an autopsy upon an individual who had died of tuberculosis. The second case was a child of twelve years of age operated upon by Jalaguier. The patient had had several attacks of appendicitis. The carcinoma, which was of the adenomatous type, was located at a point of the appendix at which a stenosis had resulted from the chronic inflammatory process. The rest of the appendix presented the usual appearance of acute appendicitis. The patient made a good recovery.

Giscard,[20] in 1900, reported a case of a man of thirty-seven years who in March, 1898, had his first attack, which was mild in character. In October of the same year he had a second attack, and after several days developed grave symptoms, which led to an operation. An abscess of the right iliac fossa was found with local peritonitis. The appendix was situated behind and to the inside of the cæcum. The patient made a good recovery. The appendix was about the size of a crayon of chalk, and the lumen was obstructed at about the middle of the organ by what appeared to be a cicatricial thickening. In the distal end of the appendix there was some pus. Histological examination of the appendix showed both a catarrhal and chronic inflammation. At one point the sections also showed a narrowing of the lumen by a neoplasm situated between the mucosa and musculature. This growth occupied about one-half of the circumference of the appendix, and

caused a projection towards the lumen as well as towards the periphery. The carcinoma seemed to originate from the deeper layer of the glands, and in its superficial portion presented the characteristics of an adenocarcinoma, while in the deeper portion it resembled an alveolar carcinoma with cylindrical cells.

Rolleston,[21] in 1900, reported a case of a woman twenty-six years of age, operated upon during a fourth attack of appendicitis, the previous three attacks having occurred within a period of fifteen months. The appendix was slightly adherent to the posterior wall of the uterus, and on section presented a globular mass a little larger than a marble, and situated near the tip. This mass presented a caseous appearance which suggested tuberculosis. Histologically, it proved to be a spheroidal-cell carcinoma, which in places appeared to extend almost to the peritoneum. The growth was undoubtedly primary in the mucosa. Several months after the operation the patient was reported to be in poor health, and the probability of secondary growths was entertained.

Whipham,[22] in 1901, reported a case of a woman of forty-five years who was admitted to St. George's Hospital with great enlargement of the abdomen and a tumor in the left iliac fossa. Operation was deemed inadvisable, and the patient died four weeks later. At autopsy the abdomen was found to contain a large quantity of serous fluid. The peritoneum over both the parietes and viscera was thickly studded with nodules of new growth. One or two nodules were found in the liver, and the left ovary was transformed into a mass of new growth measuring six by four inches. The lymphatic glands of the neck and anterior mediastinum were also involved. The mucous membrane of the entire alimentary tract was normal, with the exception of a small portion at the base of the appendix, which was occupied by a new growth. The neoplasm proved to be a spheroidal-cell carcinoma. The writer assumed the neoplasm to be primary in the appendix because of the absence of new growths elsewhere in the alimentary tract, and also because the growth was most marked in the mucosa and submucosa, and invaded the muscular coats of the appendix but slightly. The reasons for the assumption that this was a primary carcinoma of the appendix do not appear to be by any means valid, and it is much more probable that the growth originated in the left ovary and metastasized to the appendix.

McBurney,[23] in 1901, reported two cases of primary carcinoma of the appendix. The first was a case of a woman twenty-three years of age, who had had a severe attack of appendicitis two years previously. The symptoms subsided in ten days, and the patient remained well except for a feeling of pain and discomfort in the right iliac fossa on movement or active exercise. Two months before operation the pain became very severe and incapacitated the patient, without rise of temperature or pulse. On examination the patient appeared to be in good health, but the appendix was very sensitive. At operation the appendix was found free from adhesions or disturbance of the peritoneal surface. The organ was four inches in length, much thickened and enlarged, and presented two strictures, one near the base and one near the tip. Near the tip was a small tumor about the size of a green pea, of dense consistency and white color, which microscopically proved to be a pure carcinoma. There was no evidence of malignant disease elsewhere in the body. The second case was of a man of about thirty years who had given no history of appendicitis. At autopsy the appendix was found to present a rounded tumor near the tip. This tumor was considerably larger than that in the first case, and microscopically was found to be a pure carcinoma resembling the first specimen.

Goffe,[24] in 1901, reported a case of a Jewess of fifteen years, well developed and well nourished, who for more than a year had complained of pain in the region of the appendix after exercise. A clinical diagnosis of chronic appendicitis was made and the organ removed. The appendix was unusually long, thickened, and tortuous, and in the extreme tip was a small white tumor the size of a large pea. Microscopically, the tumor resembled a fibroma, and appeared to have developed in the wall of the appendix and protruded into the lumen. Histologically, it was found to be a carcinoma, which did not, however, invade the muscular coats.

Kelly,[25] in 1901, reported three cases of primary carcinoma and one case of primary endothelioma of the appendix. In the first case the appendix presented the usual character of acute ulcerative appendicitis. At about the junction of the middle and distal thirds was a tumor six millimetres in diameter, occupying chiefly the mucosa and submucosa, and microscopically of the type of carcinoma simplex. The second case was that of an indi-

vidual twenty-four years of age, with a history of four attacks of appendicitis in the year previous to operation. At operation the appendix was free from adhesions, nine centimetres in length and from five to seven millimetres in diameter. There was no macroscopical evidence of tumor formation; microscopically, however, there was an area near the base of the organ which presented an appearance which the writer considered to be endothelioma. The description of the specimen, together with the uncertain position of this group of tumors, leaves some doubt as to whether this may not have been a case of carcinoma rather than endothelioma. The third case was that of a man of nineteen years who had always been strong and well. Eight days before admission to the hospital he had been taken with severe abdominal pain, which localized itself in the right iliac fossa, where a mass about three inches in diameter could be felt. At operation a collection of pus was found around the head of the cæcum and the base of the appendix. The appendix was five centimetres in length and one centimetre in diameter. Histologically, the organ presented the lesions of ulcerative appendicitis, in addition to which there was a small growth situated near the base of the appendix. The growth, which was of the type of carcinoma simplex, was located almost entirely within the submucosa, although in a few places there was a slight infiltration of the muscular coats. The fourth case was of a man of sixty-three years, who had always been well until a short time before admission to the hospital, when he began to have attacks of rather severe pain in the right iliac fossa. At operation the appendix was found to be adherent to the surrounding structures, and both the appendix and intestines were studded with numerous whitish nodules suggestive of miliary tubercles. The retroperitoneal glands were also enlarged. The patient died seven days after operation, but no autopsy was obtained. The appendix was two centimetres in length and varied in diameter from one to two centimetres. It presented a constriction at about the middle. Microscopically, the lumen was obliterated, and there was no evidence of a mucous membrane in any part of the organ. The submucosa, muscularis, and peritoneum were infiltrated with nests of carcinoma cells. The meso-appendix was similarly infiltrated. The writer suggests the possibility that the appendix was involved secondarily to carcinoma somewhere else in the body; but the absence of the mucosa and the arrangement of the car-

cinoma cells inclined him to the view that the growth was primary in the appendix. In view of the fact, however, that there was general peritoneal involvement which was also evident upon the surface of the appendix, together with involvement of the retroperitoneal glands, it would seem very much more probable that the growth in the appendix was secondary to a neoplasm elsewhere in the body.

Harte and Willson,[26] in 1902, have reported two cases of primary carcinoma of the appendix. The first case was of a woman of twenty-four years, who at the age of nineteen had an attack of what appeared to be appendicitis, from which she recovered and remained well for four years, when she had another attack. For several months prior to the operation she had had more or less pain in the region of the appendix. On physical examination there was abnormal sensitiveness in the right iliac fossa and some thickening of the tissues about the appendix. At operation the appendix was found to be free from adhesions and to project upward behind the cæcum. It was fifteen centimetres in length, contained two small concretions, and appeared normal to the naked eye. The lumen was, however, obliterated for almost the entire length of the organ. On physical examination a scirrhous carcinoma five millimetres in diameter was found about one centimetre from the tip. The carcinoma appeared to have originated from the remains of the glands of the mucosa and to have invaded all the coats of the appendix. The second case was of a man of twenty-five years, who for eight months prior to the operation had had more or less continuous pain in the right iliac fossa. The appendix was found to be bound down behind the cæcum by old adhesions. It contained a concretion about the size of a grape-seed and presented a perforation near the tip. Sections of the appendix about one centimetre from the tip showed a carcinoma taking its origin from the mucosa. All the coats of the appendix were involved in the growth, which was a carcinoma simplex in type. In addition, the appendix presented the gross and microscopical appearance of acute suppurative appendicitis.

Weir,[27] in a discussion of primary carcinoma of the appendix at the meeting of the American Surgical Association in 1902, briefly reported one case which had occurred in his practice. There was, however, no description of the gross or microscopical appearance of the tumor.

Jessup,[28] in 1902, reported a case of a woman of thirty-six years who had had considerable pain in the left inguinal region following an abortion. Operation was undertaken by Dr. Cleveland for disease of the uterine adnexa. A cyst of one ovary was found, and the appendix, which was bound down by adhesions, was removed. The appendix was six centimetres in length, and at the junction of the middle and distal thirds was bent at a right angle, with a constriction at the bend, beyond which was an enlargement. The diameter of this portion was one centimetre while that of the proximal portion was five millimetres. The lumen was obliterated at the bend, and the enlarged portion was occupied by a firm tumor mass, the muscular coat presenting a thin shell. Microscopical examination showed the tumor to be an adenocarcinoma which had infiltrated the mucosa, submucosa, and muscularis. The middle and proximal portions of the organ were free from new growth. There had been no symptoms pointing to disease of the appendix, and the discovery of the carcinoma was accidental.

Of the forty cases here referred to, it would appear that eight were probably not cases of primary carcinoma of the appendix. These eight comprise one case of Merling, one case of Prus, one case of Kolaczek, one case of Bierhoff, one case of Draper, one case of Monks, one case of Whipham, and one case of Kelly. To these eight cases may be added the case reported by Glazebrook as endothelial sarcoma and one reported by Kelly as endothelioma; although it would seem, from the description, that these may have been instances of primary carcinoma of the appendix. Of the remaining thirty cases there may be some question as to the authenticity of the four cases reported by Rokitansky, the three cases reported by Leichtenstern, the case reported by Maydl, the case reported by Nothnagel, and the case reported by Zeman, because in none of these cases was there a report of a microscopical examination or of positive proof that if a carcinoma existed it was necessarily primary in the appendix.

The remaining twenty cases would, however, appear to be fairly definitely proven to be instances of primary carcinoma

of the appendix. The macroscopical findings in these twenty cases are furthermore confirmed by more or less extensive descriptions of the microscopical characters of the neoplasms. These twenty cases comprise one case of Beger, one case of Stimson, one case of Mossé and Daunic, one case of Wright, one case of Hurdon, four cases of Letulle and Weinberg, one case of Giscard, one case of Rolleston, two cases of McBurney, two cases of Harte and Willson, one case of Goffe, two cases of Kelly, one case of Weir, and one case of Jessup.

To these the writer wishes to add the following three cases recently studied by himself.

CASE I, Figs. 1, 2, and 3.—W. D., male, aged eighty-one years, a patient of Dr. Vander Veer. The patient had always been strong and healthy until during the later years of life, when he had shown evidence of both pulmonary and cardiac disease, which were the immediate cause of death. There had never been any symptoms of disease of the appendix. At autopsy, the main lesions were pulmonary tuberculosis with pleural effusion upon the right side, general arterial sclerosis with hypertrophy and dilatation of the heart, chronic interstitial nephritis, and a primary neoplasm of the vermiform appendix. The appendix projected upward behind the cæcum, was free from adhesions, and measured five and one-half centimetres in length. The proximal two centimetres of the organ was of normal appearance and measured six millimetres in diameter. The distal three and one-half centimetres of the appendix was much enlarged and measured three centimetres in diameter. Projecting from the convex surface of the enlarged portion of the appendix at about the middle of the surface, opposite the mesenteric attachment, was a mass of yellowish-green, translucent, gelatinous material. This mass measured two and one-half by two and one-half by two centimetres in its diameters, and presented an irregular contour. On transverse section of the appendix through the middle of the enlarged portion, the lumen of the organ was found to be filled with a gelatinous substance resembling that already mentioned. At about the middle of the convex surface of the enlarged portion of the appendix and opposite the mesenteric attachment was a perforation one centimetre in diameter, through which the gelatinous

FIG. 1.—Case I., primary colloid carcinoma of appendix. Showing the projection of the colloid material through a perforation of the organ. (Natural size.)

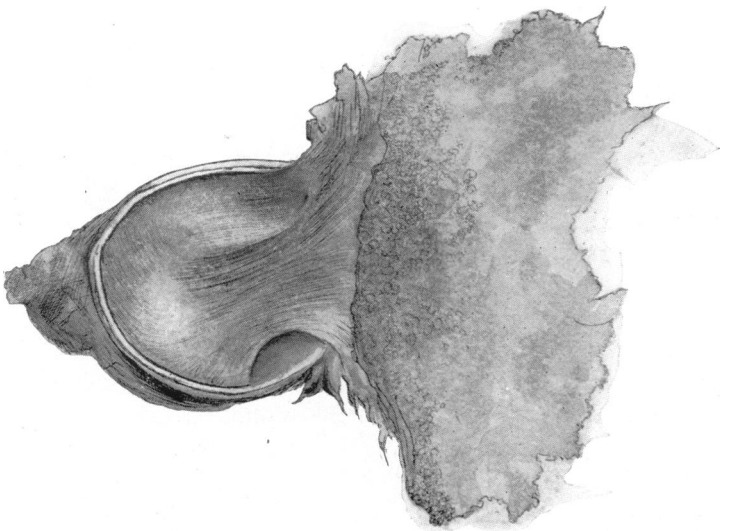

FIG. 2.—Case I., primary colloid carcinoma of appendix. Transverse section through the appendix in the region of the perforation. (Natural size.)

material in the lumen of the organ was continuous with that already described as attached to the surface. The perforation was definitely circumscribed and the edges were rather firm. There was no evidence of necrosis of the tissue about the perforation. The gelatinous substance within the appendix presented a striated appearance, the striæ tending to converge towards the perforation. This gelatinous material could be readily detached from the wall of the appendix, and in places presented a decidedly lamellated appearance in addition to the striation already mentioned, and the consistence was about that of calves'-foot jelly. The wall of the appendix, except in the region of the perforation, appeared distinctly thickened, and presented the appearance of an hypertrophy of the musculature. Careful examination of all the other viscera of the body, as well as of the regionary lymphatic glands, failed to reveal any other focus of new growth.

Microscopical examination of sections stained in hæmatoxylin and eosin, as well as van Gieson's stain, did not reveal in any portion of the dilated appendix any evidence of the mucosa. This appeared to be mainly due to an atrophy of the mucosa, resulting from the pressure of the contents of the organ and to a much lesser extent to a destruction of the mucosa by a new growth, which in places could be seen invading both the submucosa and the musculature, but nowhere invading the deeper layers of the musculature or peritoneum, except in the vicinity of the perforation. The new growth presented the typical appearance of an adenocarcinoma, which, however, was evident only in the most recent portions of the growth, and was in no place at all abundant. The new growth was composed of glandular structures which were closely arranged, with but very little stroma. The glands were lined by a high columnar epithelium, the protoplasm of which stained well. In the most recent portions of the growth there was but little evidence of the gelatinous material; but as one traced the glandular structures into the older portions, the columnar epithelial cells became much elongated and the protoplasm stained faintly. The limiting membrane of certain of the cells appeared to have burst, and the contents were extruded into the lumen of the gland. The nuclei of the cells stained less deeply, and began to show slight evidences of fragmentation and disintegration. Gradually the cells became transformed into the gelatinous material, until in older portions of the tumor the indi-

vidual cells could no longer be distinguished and the nuclei, fragmented and disintegrated, were scattered in an irregular row along the few strands of stroma, while practically the entire gland spaces were occupied by the gelatinous material. Still older portions of the new growth, which to the naked eye appeared to be composed almost entirely of gelatinous material, presented somewhat of a lamellated appearance, the lamellæ being composed of the gelatinous material, while between the lamellæ vestiges of the stroma could be distinguished, associated with which were bits of the fragmented nuclei of the tumor cells. In the oldest portions of the tumor these lamellæ were closely packed together; the result, evidently, of pressure caused by the constant production of the material by the new growth. Between these lamellæ, which corresponded to the much altered gland spaces, the stroma could no longer be distinguished and the fragmented nuclei had entirely disappeared. In the place of the stroma and fragmented nuclei there was a small quantity of rather granular material, which stained deeply with eosin and was probably hyaline in character. The new growth appeared to be fairly well localized in the region of the perforation and did not involve the wall of the appendix at all extensively. Inasmuch, therefore, as there was no evidence of the neoplasm in other parts of the body, the conclusion would seem to be justified that this was a case of primary adenocarcinoma of the appendix belonging to the type which is usually known as colloid carcinoma.

CASE II, Fig. 4.—Mrs. L., aged thirty-six years, a patient of Dr. Macdonald. The patient had always enjoyed good health until about eight years previously, when she had an attack of what was called "peritonitis," from which she made a fairly good recovery, and had enjoyed good health until a short time before the operation, when she developed symptoms of pelvic disease. The patient had never manifested any evidence of disease of the appendix. At the operation a cyst of the right ovary was found associated with rather extensive pelvic inflammatory disease, for which bilateral salpingo-oöphorectomy was done. The appendix was free from adhesions and did not present any definite evidence of disease, but was removed in the course of the operation. The patient made an uneventful recovery, and has remained in perfect health ever since, the operation having been done in 1900.

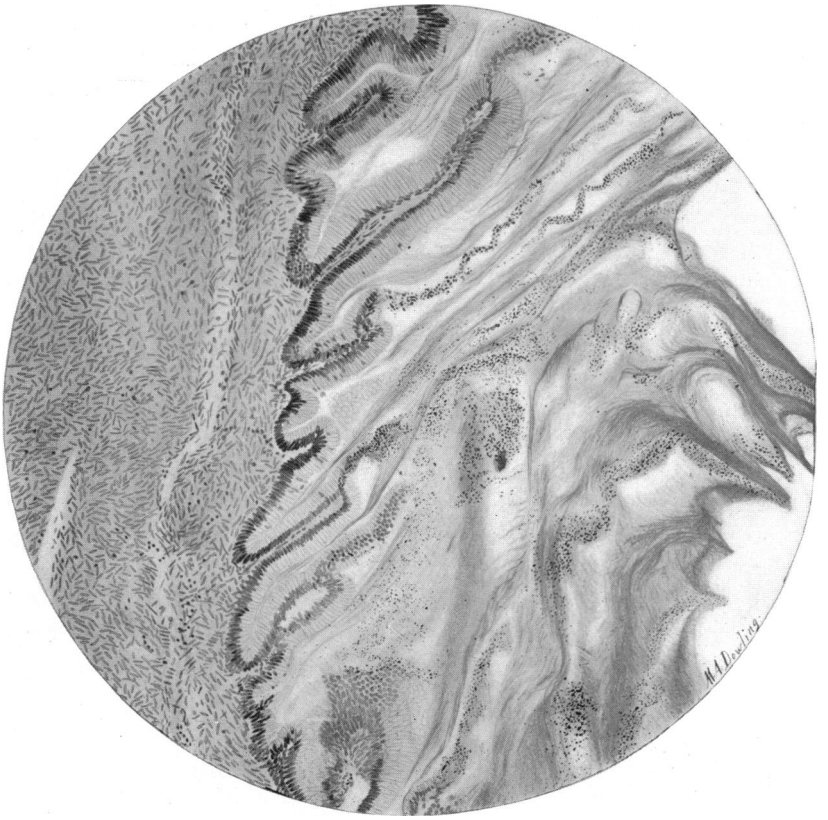

FIG. 3.—Case I., primary colloid carcinoma of appendix.

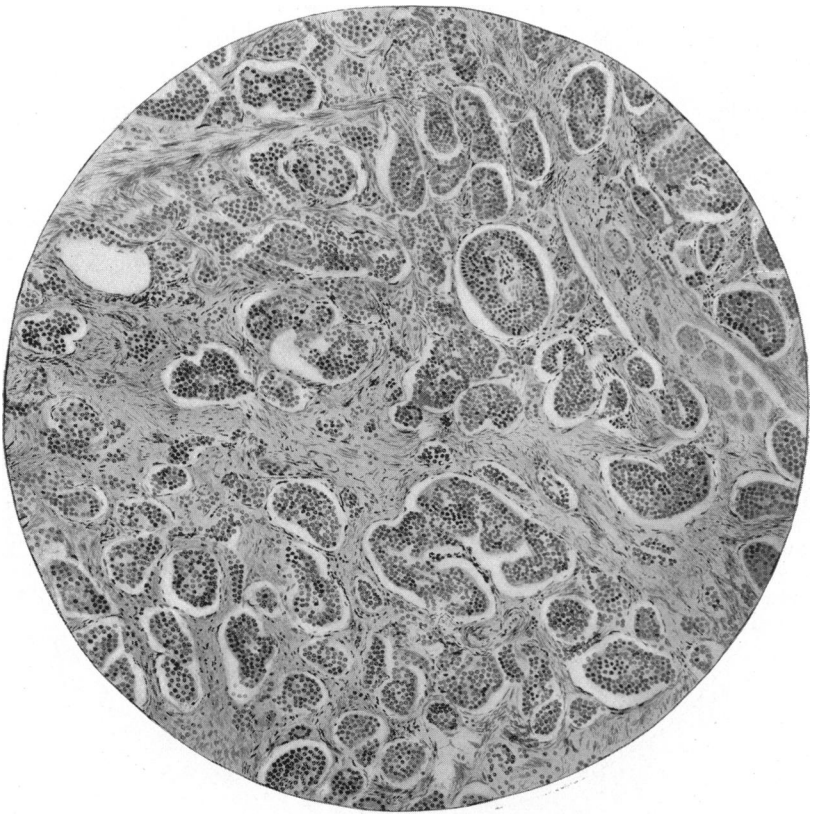

FIG. 4.—Case II., primary carcinoma of an obliterated appendix.

The appendix measured four centimetres in length and ranged from six to nine millimetres in diameter. The mesentery, which contained a considerable amount of fat, extended to the tip; the peritoneum was smooth and glistening; the vessels, however, were somewhat congested. Situated about one centimetre from the proximal end of the appendix was a slight enlargement which extended for about eight millimetres. It was in this region that the organ presented the greatest transverse diameter. The consistency of this portion resembled that of the rest of the appendix, which was decidedly firm. The lumen was completely obliterated throughout the entire organ. Transverse section of the base and tip of the appendix showed the lumen to be obliterated by a white reticulated tissue, in the meshes of which collections of fat could be seen. The muscular coat appeared to be normal.

Section through the enlargement already referred to showed the central portion of the organ to be occupied by a more homogeneous tissue, which in the specimen hardened in Orth's fluid presented a slight yellowish tinge. This tissue appeared to extend into the musculature, especially upon the side of the mesenteric attachment. Microscopical examination of sections through the proximal and distal portions of the appendix stained in hæmatoxylin and eosin showed the usual appearance of chronic obliterative appendicitis. The lumen could not be distinguished, and its place, as well as that of the mucosa, was occupied by rather loose connective tissue continuous with the submucosa. No vestiges of the mucosa, glandular structures, or lymphoid apparatus of the appendix could be distinguished. The muscular coats were somewhat thickened and hypertrophied, and the peritoneum was also slightly thickened. In sections through the enlargement of the appendix already mentioned the central portion of the organ was found to be rather densely infiltrated with a new growth, which involved to a lesser extent the musculature and peritoneum. The growth was characterized by numerous large and small alveoli occupied by cells, the outlines of which could be distinguished with difficulty, but which appeared to be for the most part cuboidal or polygonal in shape. These cells contained rather large round or oval nuclei, most of which stained well in the hæmatoxylin, but some of which were rather vesicular in character. The cells and nuclei appeared to be of fairly uniform size, and in most of

the alveoli were densely packed together. Some of the alveoli were so small as to present only three or four cells in transverse section. In many of the larger alveoli the process of fixing and hardening the tissue had caused the cells to shrink away *en masse* from the connective-tissue stroma, leaving a clear space. In certain of the alveoli a distinct lumen could be distinguished surrounded by one or two rows of cuboidal cells. Some of the larger alveoli contained a considerable number of red blood-corpuscles which may have found their way there either from trauma at the time of the operation or from invasion of the blood-vessels by the new growth, which in some places was quite evident. The protoplasm of the cells in some of the alveoli presented a small amount of rather diffuse yellowish-brown pigment. The outer or longitudinal layer of muscle appeared to be more extensively involved than the inner or circular layer, and both layers were most extensively involved on the side of the mesenteric attachment. The peritoneum, which was decidedly thickened, also presented numerous alveoli of tumor cells. The tumor was not circumscribed, but appeared to extend rather diffusely through the structures of the appendix, and appeared in places to extend along the blood and lymph channels. In general, the tumor appeared to be epithelial in character, although there were certain portions of it in which an endothelioma of blood-vascular origin was strongly suggested. It is our belief, however, from a careful study of many sections, that the tumor was a carcinoma of a somewhat alveolar type, and was undoubtedly primary in the appendix.

CASE III.—F. C., male, aged nineteen years, a patient of Dr. Macdonald, was admitted to the Albany Hospital, June 9, 1902, complaining of general abdominal pain. The family history was negative, as was the patient's past history. He had always been strong and healthy until the onset of the present illness.

The present illness began in January, 1902, with an attack of acute appendicitis, which was associated with the formation of an indurated mass in the right iliac fossa, in which after a short time an abscess formed, which opened externally in the right lower quadrant of the abdomen. The sinus still existed when the patient was admitted to the hospital. The tumor mass on the right side never disappeared, and the discharge from the sinus was fairly continuous. The patient had lost forty pounds in weight. There were no symptoms associated with the fistula

which suggested a communication with the bowel. No diarrhœa, but at times constipation. The patient had had more or less continuous pain in the right iliac fossa for several months prior to admission to the hospital. The fæces had never shown any abnormal appearance.

On admission the patient presented a well-marked tumor mass in the right iliac fossa, the size of a large fist. This mass was tender on palpation, and from the sinus there was a purulent discharge. A clinical diagnosis of tuberculosis of the head of the cæcum was made. The patient was operated upon June 11, 1902.

At operation the mass in the right iliac fossa was found to be composed of a new growth involving the appendix, cæcum, ileum, the ascending and a portion of the transverse colon, as well as a loop of the jejunum. All of the involved parts were adherent in a mass. It was found necessary to remove the entire cæcum with the remains of the appendix, and about eleven centimetres of the ileum and ascending, as well as of a portion of the transverse colon, and about eighteen centimetres of the jejunum. The appendix was almost entirely destroyed, and the lumen of the proximal portion opened freely into an abscess cavity the size of a small hen's egg, which contained and was lined by necrotic material, and which communicated with the fistula which opened upon the surface of the abdomen. The appendix and the tissues immediately surrounding it appeared to be the oldest portions of the new growth. There was also extensive involvement of the regional lymphatic glands, which were removed so far as possible. The severed ends of the jejunum were united by a Murphy button with secondary Lembert sutures. The end of the transverse colon was closed, while the end of the ileum was brought out into the wound. The patient did fairly well for about two weeks, when he began to grow weaker, and died of inanition.

The specimen removed at operation consisted of the cæcum, the remains of the appendix, about eleven centimetres of the ileum, the ascending and a portion of the transverse colon, and some enlarged lymphatic glands in one mass, while in a separate mass were about eighteen centimetres of the jejunum. The distal portion of the appendix was entirely destroyed, while the proximal two centimetres of the organ could still be distinguished. The lumen opened freely into a small cavity two and one-half

centimetres in diameter, situated between the ileum and the cæcum. This cavity was located in the mass of new growth, which appeared to correspond to the distal portion of the appendix, and which seemed to be the oldest portion of the tumor. The lumen of the appendix opened freely into the cæcum as well as into the small cavity already described. To this mass of new growth the lower portion of the ileum as well as the ascending and transverse colon were adherent, and were apparently extensively involved. The growth had caused an ulceration through the wall of the ileum as well as of the transverse colon, both of which perforations opened into the cavity already referred to. The new growth was very much more extensive in the peritoneal and muscular coats of the involved bowel than in the mucosa, and it seemed apparent that the adherent intestines had become involved secondarily. The new growth was of rather soft consistence, and on section of a grayish-white color, and appeared to be largely composed of a gelatinous translucent material resembling colloid. In portions of the tumor there was also marked necrosis and softening. The gelatinous material was contained in more or less definite spaces, separated by bands of connective tissue. The lymphatic glands were much enlarged and diffusely involved by the new growth, which presented extensive colloid degeneration.

Microscopical examination of sections through the base of the appendix stained in hæmatoxylin and eosin showed a decided thickening of all the coats of the organ, due to a diffuse infiltration by a new growth. The lumen contained a small amount of necrotic material. The lining epithelium had disappeared, but certain of the glands as well as some of the lymphoid tissue of the mucosa could still be distinguished. The new growth was for the most part of a somewhat glandular type and presented larger and smaller alveoli, which in the more recent portions of the growth were occupied by irregular shaped cells, most of which were cuboidal or polygonal in shape. In some of the alveoli a definite lumen could be distinguished, while in others none could be seen, and the entire alveolus was packed with epithelial cells. In some of the places there was a slight resemblance between the glands of the mucosa and the more recent portions of the growth. In certain portions the tumor was composed simply of narrow columns of epithelial cells, suggesting the appearance seen in carcinoma simplex. In older portions of the growth the alveoli

were much larger, and the epithelial cells were grouped along the periphery of the alveolus, while the central portion was occupied by a homogeneous substance which stained very faintly with hæmatoxylin, and which presented a marked reticulated appearance, and in which an occasional degenerated epithelial cell or nucleus could be seen. In still older portions of the growth several alveoli had apparently fused, and the intervening stroma as well as the fixed tissue in general had largely disappeared. Most of the epithelial cells had degenerated, and the alveoli were filled with colloid material, scattered through which were occasional more or less degenerated epithelial cells and free nuclei. The colloid material first appeared as small refractile globules in the protoplasm of the tumor cells. These globules enlarged and became fused, as a result of which practically the entire cell came to be occupied by the colloid material, which stained very faintly with hæmatoxylin. The nucleus of the cell either entirely disappeared or was pushed off to one side of the cell, presenting the signet-ring appearance. The cell membrane in many instances appeared to remain intact, but sooner or later ruptured, and the colloid material became fused with that resulting from the degeneration of neighboring cells. In the oldest portions of the tumor practically all the cells had undergone the colloid degeneration, and the alveoli were occupied simply by the colloid material without, in many instances, a single distinguishable epithelial cell or nucleus. These alveoli showed a marked tendency to fuse, thus giving rise to extensive areas of colloid material. The colloid substance presented a markedly reticulated appearance, part of which seemed to be due to the preservation of more or less of the cell membrane as well as some of the intervening stroma. There were, however, in the oldest portions of the tumor but comparatively little stroma and very few blood-vessels. The lymphatic glands were diffusely infiltrated with the new growth, and only a small zone of the lymphoid tissue remained immediately beneath the capsule. The colloid degeneration was even more marked in the lymphatic glands than in the tumor itself, and practically all of the new growth appeared to have undergone this degeneration.

From a careful, clinical, anatomical, as well as pathological investigation of this case, we feel justified in assuming that it was a primary colloid carcinoma of the appendix of an adenomatous type, with extensive secondary involvement of the neigh-

boring portions of the intestines, as well as the regional lymphatic glands.

The early view was that carcinoma of the appendix was not primary, but resulted from extension from some neighboring organ. On the contrary, recent investigation has shown that primary carcinoma of the appendix is of more frequent occurrence than is ordinarily supposed, while secondary tumors of the appendix are of rare occurrence, even though the cæcum may be extensively involved.

Regarding the etiology of carcinoma of the appendix comparatively little is known, although recent studies have shown that in some instances, at least, it is one of the sequelæ of chronic inflammation of that organ. Theoretically, the appendix should frequently be the site of carcinoma, because certain factors which are usually supposed to bear an important causal relationship to the development of neoplasms are in evidence in this organ. In the first place, carcinoma of the gastro-intestinal tract tends to originate at those portions which are narrow or constricted, which is one of the characteristics of the appendix. Secondly, fœtal remains as well as atrophying organs appear to be more prone to the development of carcinoma, and such a condition is supplied by the appendix. Thirdly, mechanical irritation, which is such an important factor in the development of certain neoplasms, exists extremely frequently in the appendix, and usually results from the action of enteroliths, dried fæcal matter, and occasionally foreign bodies. When one considers the great frequency with which gall-stones are followed by the development of carcinoma of the gall-bladder or bile passages, it seems extremely remarkable that such a condition is not more frequently observed in the appendix. Fourthly, chronic inflammation, which in so many instances is followed by the development of neoplasms, occurs almost as frequently in the appendix as in any organ of the body. The studies of Letulle and Weinberg, Harte and Willson, and others have shown that primary carcinoma of the appendix does occasionally develop in an organ the subject of chronic inflamma-

tion, usually of the obliterative type. Of such a character is Case II reported by the writer, in which a typical carcinoma had developed in a completely obliterated appendix. It may furthermore be urged that if more careful routine examination were made of appendices removed at operation, primary carcinoma would be observed more frequently, for in many of the cases reported during the past few years the new growth has been an accidental find, the presence of which was never suspected before operation, or even, in some instances, after macroscopical examination of the organ. It is only comparatively recently that many surgeons have made a practice of having all appendices removed at operation examined by a pathologist, and this certainly accounts for the increased number of neoplasms of this type observed of late. Sections should be studied not merely from one or two portions of the organ, but from several portions, and especially in those appendices which show evidences of chronic inflammation.

A striking feature of many of the cases of primary carcinoma of the appendix reported is the development of the disease in comparatively early life.

Of the twenty-three cases in which the proof seems conclusive that the new growth was primary in the appendix, the age of the patients is stated in seventeen. Nine of these seventeen, or 53 per cent. of the patients, were under thirty years of age, while four, or 24 per cent., were under twenty years of age. The youngest case reported was that of a child of twelve years. The early age at which such a large percentage of the cases occurred may be assumed to bear a definite relationship to the age at which appendicitis is most frequent. For, as is well known, the great majority of cases of appendicitis occur in individuals under thirty years of age, and an especially large percentage of the cases are under twenty.

Carcinoma of the appendix may belong to any of the ordinary types of that neoplasm, although the colloid type appears to occur more frequently than any other. In Cases I and II reported by the writer the neoplasms were of that variety. In a considerable number of the cases reported the new growth

was confined to the appendix, and did not present any evidence of either extension or metastasis. This was very likely due to the fact that most of the tumors were removed in a comparatively early stage. The tumor may attain considerable size and may ulcerate through the wall of the appendix, and thus give rise to a local or general peritonitis. It may also give rise to a focus of suppuration, which may present the usual characters of an appendicular abscess. By local extension neighboring portions of the intestines or other viscera may become involved, and the pathological picture will depend largely upon the extent of this involvement.

In the great majority of cases the diagnosis of carcinoma of the appendix is impossible. Writers have even gone so far as to state that it is practically *always* impossible. In some of the cases there are no symptoms whatever pointing to the appendix, and the tumor is an accidental find either at operation or autopsy, as instanced by Cases I and II reported by the writer. When symptoms are present, they are usually those of appendicitis of the chronic relapsing type. In some instances the new growth may apparently cause an acute attack of appendicitis, and a perforation may result, usually at the site of the tumor. Pain is perhaps the one symptom present in the majority of the cases. This is usually referred to the right iliac fossa and may be of very varied character. When present, it differs in no way from that associated with chronic appendicitis, and hence the diagnosis is usually of that condition. The pain is usually due to the mechanical action exercised by the tumor. In the later stages a well-defined tumor mass may present in the right iliac fossa which strongly resembles an appendicular abscess. When it attains considerable size, the tumor often shows a tendency to be associated with the formation of an abscess, which may open externally, and a discharging sinus is formed which shows no disposition to heal. From such a sinus gas and fæcal contents may be discharged, though this is very exceptional. The existence of such a condition with normal defecation might speak in favor of a neoplasm of the appendix. Diarrhœa and constipation, or both, may also occur in the later

stages, but they are usually due to the extension of the tumor into the neighboring intestines, and are in no sense the result of the new growth in the appendix itself.

The treatment of the condition is exclusively operative, and since the association of the new growth with the inflammatory process in that organ has come to be so well recognized, there is an added reason for the extirpation of those appendices which present evidences of either acute or chronic inflammation.

From a careful study of the subject, the following conclusions may be drawn:

1. Primary carcinoma of the appendix is not of such rare occurrence as has been hitherto supposed.

2. Every appendix removed at operation or autopsy, if it presents any evidence whatever of disease, should be examined most carefully, and sections should be made from several portions of the organ for microscopical study.

3. The relationship of primary carcinoma of the appendix to chronic appendicitis, especially of the obliterative type, seems to be fairly definitely established.

4. Primary carcinoma of the appendix shows a tendency to develop at a comparatively early period of life.

5. Primary carcinoma of the appendix does not show a marked tendency either to extension or to metastasis.

6. The symptoms of primary carcinoma of the appendix are usually the symptoms of appendicitis of the chronic type.

7. The diagnosis of primary carcinoma of the appendix is in the great majority of cases impossible.

8. The treatment of the condition should always be operative.

[The writer wishes to acknowledge his indebtedness to Dr. W. W. Sanford and Miss M. A. Dowling for the drawings published in connection with this article.]

LITERATURE.

[1] Merling. Journal de l'expérience, 1838.

[2] Prus. Thesis of Croizet, Paris, 1865.

[3] Rokitansky. Medicinische Jahrbücher, 1867, xiii, p. 179; also Wiener, Medicinische Wochenschrift, 1866, xvi, p. 863.

[4] Kolaczek. Archiv für klinische Chirurgie, 1875, xviii, p. 366.
[5] Leichtenstern. Ziemssen's Handbuch, 1876, vii, 2, p. 524.
[6] Bierhoff. Deutsche Archiv für klinische Medicin, 1880, Band xxvii.
[7] Beger. Berliner klinische Wochenschrift, 1882, xix, p. 616.
[8] Maydl. Ueber die Darmkrebs, Wien, 1883.
[9] Draper. Boston Medical and Surgical Journal, 1884, cx, p. 131.
[10] Lafforgue. Des tumeurs primitives de l'appendice Vermiculare, Thèse de Lyon, 1893.
[11] Glazebrook. Virginia Medical Monthly, 1895, xxii, p. 211.
[12] Stimson. ANNALS OF SURGERY, 1896, xxiii, p. 186.
[13] Letulle and Weinberg. Bulletin de la Société Anatomique de Paris, 1897, lxxii, p. 747.
[14] Mossé and Daunic. Bulletin de la Société Anatomique de Paris, 1897, lxii, p. 814.
[15] Wright. Boston Medical and Surgical Journal, 1898, cxxxviii, p. 150.
[16] Monks. Boston Medical and Surgical Journal, 1899, cxl, p. 210.
[17] Nothnagel. Specielle Pathologie und Therapie, 1898, xvii, p. 631.
[18] Hurdon. Bulletin of the Johns Hopkins Hospital, 1900, p. 175.
[19] Letulle and Weinberg. Communication à la Société Anatomique de Paris, du 22, Fevrier, 1900.
[20] Giscard. Toulouse, Imp. St. Cyprien, 1900, 8vo, No. 360, p. 51.
[21] Rolleston. London Lancet, July 7, 1900.
[22] Whipham. London Lancet, February 2, 1901.
[23] McBurney. New York Medical Record, September 21, 1901, p. 478.
[24] Goffe. New York Medical Record, July 6, 1901.
[25] Kelly. Transactions of the Pathological Society of Philadelphia, 1901.
[26] Harte and Willson. Transactions of the American Surgical Association, 1902.
[27] Weir. Transactions of the American Surgical Association, 1902.
[28] Jessup. New York Medical Record, August 23, 1902.